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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/040,416	01/09/2002	Tetuya Ookura	217969US0X CIP	3704

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EXAMINER	
PAK, YONG D	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 10/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/040,416	OOKURA ET AL.	
	Examiner	Art Unit	
	Yong D Pak	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-54* is/are pending in the application.

4a) Of the above claim(s) *1-9,17-30, 35-46 and 51-54* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-16,31-34 and 47-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/26/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application is a CIP of 09/800,487, now abandoned.

The amendment filed on August 16, 2004, amending claims 1-3, 5, 7-11, 13, 15-19, 21 and 23-26 and adding claims 27-54, has been entered.

Claims 1-54 are pending.

Election/Restrictions

Applicant's election with traverse of Group IV in the reply filed on August 16, 2004 is acknowledged. The traversal is on the ground(s) that the examiner has not provided any reasons or examples for restriction the claims into Groups I-XII but has only provided general assertions. This is not found persuasive because adequate reasoning was given.

The DNA molecules of Inventions II, IV and VI encoding proteins having different structures. It is a well established scientific principle that structure of a protein determines the functional characteristics of the protein. Therefore, the DNA of Inventions II,IV and VI are patentably distinct. A separate search is required for the DNA of Invention II, IV and VI since they have different structure.

Similarly, the protein of Inventions I, III and V are patentably distinct. A separate search is required for the DNA of Invention II, IV and VI since they have different structure. A separate search the encoded proteins of Inventions I, III and V.

Regarding the restriction between Groups (I and VII), (III and VIII) and (V and IX), MPEP 806.05(h) states that the examiner should provide an example, but the example need not be documented. The example given was that the product as claimed can be used in a materially different process, i.e. the production antibodies against the protein. This example is adequate.

Similarly, regarding the restriction between Groups (II and X), (IV and XI) and (VI and XII), MPEP 806.05(h) states that the examiner should provide an example, but the example need not be documented. The example given was that the product as claimed can be used in a materially different process, i.e. the production of the encoded protein. This example is adequate.

Regarding the restriction between Groups (VII-IX) and (X-XII), Groups VII-IX use different products, Inventions I, III and V and therefore, the inventions are drawn to methods employing patentably distinct products. Similarly, Groups X-XII use different products, Inventions II, IV and VI and therefore, the inventions are drawn to methods employing patentably distinct products.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-9, 17-30 and 35-54 withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on August 16, 2004.

Notice of Possible Rejoinder: The Examiner notes that if claims 10-16 and 31-34 are found directed to an allowable product, then claim 41, which are directed to the process of making or using the patentable product, respectively, previously withdrawn from consideration as a result of a restriction requirement, would now be rejoined pursuant to the procedures set forth in the Official Gazette notice dated March 26, 1996 (1184 O.G. 86; see also MPEP 821.04, *In re Ochiai,* and *In re Brouwer*). Since process claim 41 would be rejoined and fully examined for patentability under 37 CFR 1.104, applicants are instructed to amend said claims as deemed necessary according to rejections made against the elected claims.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on April 26, 2002 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 10-16 are rejected under 35 U.S.C. 101 because the claimed invention is directed to a non-statutory subject matter.

Claims 10-16 and 31-34, as written, do not sufficiently distinguish over nucleic acids as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See Diamond v. Chakrabarty, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "Isolated" or "Purified" as taught by the specification. See MPEP 2105.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 10-16 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 10 and 15-16 are drawn to DNA encoding an erythrose reductase from any source wherein one or more amino acids of SEQ ID NO:4 are modified by deletion, addition, insertion, or substitution. The single species erythrose reductase of SEQ ID NO: 4 is insufficient to describe the whole genus containing a vast number and combinations of amino acid deletions, insertions, additions, or substitutions. The specification fails to place limitations on the erythrose reductase structure or disclose which amino acid(s) of SEQ ID NO: 4 can be safely modified and still impart erythrose reductase activity. Therefore, the specification fails to describe other representative species from other sources or by identifying characteristics or structural properties other than the functionality of encoding a polypeptide with erythrose reductase activity.

Claims 11-14 are drawn to a DNA sequence comprising fragments of SEQ ID NO:3 (see interpretation of claims 11-14 below in the 112, 2nd paragraph rejection). The are drawn to a DNA molecule encoding a polypeptide with no limitations to the function of the encoded polypeptides. Therefore, the claims are drawn to a large variable genus of polynucleotides encoding polypeptides having unknown activity or inactive variants. The specification does not describe the function of all the polypeptide sequences derived or modified from SEQ ID NO:4 and therefore, many functionally unrelated polynucleotides are encompassed within the scope of these claims. Therefore, applicants fail to describe representative species by identifying characteristics or functional characteristics other than being fragments of SEQ ID NO:3.

Given this lack of the description of the representative species encompassed by the genus of the claims, the specification fails to sufficiently describe the claimed

invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the inventions of claims 10-16.

Claims 10-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for DNA encoding an erythrose reductase of SEQ ID NO:4, does not reasonably provide enablement for a an erythrose reductase of unknown structure and polypeptides of unknown function. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The claims encompass DNA molecules encoding polypeptides having an erythrose reductase activity with very low structural similarity to DNA encoding SEQ ID NO:4. Despite knowledge in the art for isolating polynucleotides and its encoded polypeptide, the specification fails to provide guidance regarding which amino acids of SEQ ID NO:4 are required to impart a polypeptide as an erythrose reductase. Therefore, these claims encompass DNA molecules encoding an erythrose reductase

having low structural similarity to SEQ ID NO:4. Therefore, the breadth of these claims is much larger than the scope enable by the specification.

The specification, as discussed above which places no limit to the source or structure of the DNA molecules encoding an erythrose reductase, does not support the broad scope of the claims because the specification does **not** establish: (A) regions of the protein structure which may be modified without effecting an erythrose reductase activity or the epitope-bearing portion of the protein; (B) the general tolerance to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for substitutions, deletions, insertions/additions or multiple modifications, as encompassed by the instant claims. Also, the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such

modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

Further, claims 11-14 are drawn to polynucleotides encoding polypeptides having unknown function. The claims broadly encompass not only erythrose reductase DNA sequences, but any polynucleotides comprising of fragments of polynucleotides encoding SEQ ID NO:3. Therefore, the breadth of these claims is much larger than the scope enable by the specification.

The specification does teach how to make variants of polynucleotides encoding SEQ ID NO:3. However, the function of a polypeptide cannot be predicted from its structure and the specification does not teach how to use polypeptides with unknown function. The quantity of experimentation in this area is extremely large since there is significant variability in the activity of the polynucleotides in the claims. It would require significant study to identify the actual function of the encoded polypeptides and identifying a use for the polypeptide would be an inventive, unpredictable and difficult undertaking. This would require years of inventive effort, with each of the many intervening steps, upon effective reduction to practice, not providing any guarantee of success in the succeeding steps.

The art is extremely unpredictable with regard to protein function in the absence of realizable information regarding its activity. Even very similar proteins may have every different functions. In the current case, where no specific information is know regarding the function, it is entirely unpredictable what function and activity will be found

for the protein. The prior art does not resolve this ambiguity, since no prior art activity is identified for the encoded polypeptides.

Therefore, one of ordinary skill would require guidance in order to make DNA encoding polypeptides having erythrose reductase activity with structures different from SEQ ID NO:4 and DNA encoding polypeptides having unknown function in a manner reasonable correlated with the scope of the claims. Without such guidance, the experimentation left to those skilled in the art is undue.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 10-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 11, 13, 31, 34, 47 and 50, the exact hybridization condition is unclear. Different nucleic acids hybridize to a DNA sequence under different conditions. Therefore, the scope of DNA molecules in claims 11, 13, 31, 34, 47 and 50are unclear.

Claims 11-12 are confusing because it is not clear if the functional language of "encoding a protein having an erythrose activity" belongs to both (e) and (f) or only (f). Therefore, the claims have been interpreted as the DNA sequence of (e) without the functional language and (f) with the functional language.

Further, in claim 11, in the last sentence, the article "a" is unnecessary.

Claims 13-14 are confusing because it is not clear if the functional language of "encoding a protein having an erythrose activity" belongs to both (g) and (h) or only (h).

Therefore, the claims have been interpreted as the DNA sequence of (g) without the functional language and (h) with the functional language.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 10-16, 31-34 and 47-50 are rejected under 35 U.S.C. 102(b) as being anticipated by Kita et al.

Kita et al. (form PTO-892) teaches a DNA molecule encoding an aldehyde reductase that is 54% identical to SEQ ID NO:4 of the instant invention (page 2306). The DNA molecule of Kita et al. can be construed as a DNA molecule encoding a polypeptide wherein at least one residue is modified by substitution, addition, deletion or insertion and a DNA molecule hybridizing to the fragments of SEQ ID NO:3. The functional limitation of encoding a protein having erythrose reductase activity is inherent in the encoded aldehyde reductase of Kita et al. since aldehyde reductases catalyze a variety of carbonyl compounds (page 2303 and see Kohno et al. – PTO-892 – abstract). Kita et al. also teaches a host cell comprising said DNA and a method of producing said protein (pages 2304). Therefore, the teachings of Kita et al. anticipate claims 10-16, 31-34 and 47-50.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Yong D. Pak
Patent Examiner

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